

In the Specification

Applicant presents replacement paragraphs below indicating the changes with insertions indicated by underlining and deletions indicated by strikeouts and/or double bracketing.

Please replace the paragraph beginning at page 3, line 21 through 24 with the amended paragraph as follows:

The invention involves the surprising discovery that agents that bind to the hyaluronic acid binding region of CD44 can interfere *in vivo* with adhesion, colonization, and disease caused by streptococcal bacteria. The invention also involves the discovery of the criticality of ~~does dose~~ of hyaluronic acid in preventing adhesion, colonization and disease.

Please replace the paragraph beginning at page 9, line 29 through page 10, line 12 with the amended paragraph as follows:

Fig. 3(A-D) illustrates GAS pharyngeal colonization of wild-type mice and of mice deficient in expression of epithelial CD44. (Fig. 3A and Fig. 3B) is a photomicrographic image of histologic section through the pharynx of a representative wild-type mouse stained with mAb to CD44. Immunohistochemical staining of the pharyngeal epithelium is seen with mAb to CD44 (Fig. 3A), but not with an irrelevant control mAb (Fig. 3B). Labels indicate the location of the epithelium (E), lumen (L), and submucosa (S). (B) Fig. 3C) is a table in which the left column shows the level of CD44 expression in the pharyngeal epithelium of wild-type and K5-CD44 antisense mice. Histologic sections were scored for CD44 expression in the pharyngeal epithelium by 3 independent observers without knowledge of the throat culture results. CD44 expression was graded from 1 (background) to 4 (equivalent to wild-type control). On the right are results of throat cultures for GAS on each of 5 days after intranasal inoculation with GAS B514-Sm. (C) Fig. 3D) is a histogram of summary of throat culture results presented in panel B. Data represent the percentage of mice with a positive throat culture on each day after intranasal inoculation for wild-type mice (solid bars), transgenic mice with wild-type levels of CD44 on

keratinocytes (hatched bars), and transgenic mice with reduced or absent CD44 expression on keratinocytes (open bars).

Please replace the paragraph beginning at page 10, line 13 through 16 with the amended paragraph as follows:

Fig. 4A and 4B are ~~is~~ two graphs that illustrate the prevention of GAS pharyngeal colonization in vivo by anti-CD44 monoclonal antibody. Data represent the fraction of mice with positive throat cultures for GAS on each of 3 days after intranasal inoculation with GAS administered either with mAb to CD44 (Fig. 4B) or with an irrelevant control mAb (n=20 mice per group) (Fig. 4A).

Please replace the paragraph beginning at page 10, line 17 through 21 with the amended paragraph as follows:

Fig. 5A-C are ~~is~~ three graphs that demonstrate inhibition of GAS attachment to mouse keratinocytes by exogenous hyaluronic acid. Data represent mean \pm SD of adherent bacteria recovered after incubation of keratinocytes with GAS in the presence of no inhibitor, hyaluronic acid (HA), or a control polysaccharide, alginic acid (AL), at the indicated times (Fig. 5A shows time of 0 min, Fig. 5B shows time of 45 min and Fig. 5C shows time of 120 min) after addition of GAS to the keratinocytes.

Please replace the paragraph beginning at page 10, line 27 through 31 with the amended paragraph as follows:

Fig. 8A-C are ~~is~~ three graphs that illustrate the prevention of GAS pharyngeal colonization by pretreatment with hyaluronic acid. Data represent the fraction of mice with positive throat cultures for GAS on each of 3 days after intranasal inoculation with GAS following pretreatment with phosphate-buffered saline (Fig. 8A), hyaluronic acid (HA) (Fig. 8B), or a control polysaccharide (Fig. 8C), alginic acid (AL) (n=13 mice per group).

Please replace the paragraph beginning at page 11, line 9 through 22 with the amended paragraph as follows:

Fig. 12A-C shows three bar graphs illustrating translocation of GAS through polarized keratinocyte monolayers. (Fig. 12A) the mean number of colony-forming units recovered from the medium beneath the monolayer at indicated times after inoculation of the apical surface with wild-type (solid bars) or acapsular (hatched bars) GAS. *P=0.0002 for comparison with the wild-type strain. (Fig. 12B) Internalization of GAS by keratinocytes in a polarized monolayer. At indicated time points after inoculation of the apical surface of the monolayer, extracellular GAS were killed by addition of penicillin and gentamicin, and intracellular GAS were recovered after lysis of the keratinocytes. Data represent mean colony-forming units of intracellular GAS recovered from monolayers inoculated with wild-type (solid bars) or acapsular (hatched bars) GAS. *P=0.0002 for comparison with acapsular strain. (Fig. 12C) Translocation of GAS through human skin equivalent. Data represent mean number of colony-forming units of GAS recovered from beneath a sample of human skin equivalent (see text) at various times after inoculation of the epidermal surface with wild-type (solid bars) or acapsular (hatched bars) GAS. *P=0.008 for comparison with the wild-type strain.

Please replace the paragraph beginning at page 11, line 23 through 27 with the amended paragraph as follows:

Fig. 13A-D are four drawings of which (Fig. 13A) is a syrup medicinal product (8) with syrup (12) in a container (10), (Fig. 13B) is a solid solution medicinal product (14), with a solid solution (16), and a handle (18), (Fig. 13C) is a frozen solution medicinal product (20), with a frozen solution (22), and a handle (24), and (Fig. 13D) is a semi-solid solution medicinal product (30) with a semi-solid solution (32).